REMARKS

Entry of the foregoing amendment is respectfully requested. The amendment places the application in condition for allowance, or at least in better form for an appeal should an appeal become necessary, and does not present any additional claims. Entry of the foregoing amendment, and further favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.116, are respectfully requested.

As correctly indicated in the Office Action Summary, claims 24-40 are pending in the application and are under consideration. Claims 24-40 stand rejected.

By the foregoing amendment, claims 24 and 40 have been amended. Support for the amendments to claims 24 and 40 can be found throughout the specification as originally filed, for example, at least at page 11, lines 9-13. No prohibited new matter has been introduced by way of the instant amendment. Applicants reserve the right to file a continuation or divisional application on the canceled subject matter.

Claim rejections under 35 USC § 112, first paragraph:

Claims 24-39 and claim 40 have been separately rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, has possession of the claimed invention. The rejection is respectfully traversed.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See, e.g., Moba, B.V. v. Diamond*

Automation, Inc., 325 F.3d 1306, 1319, 66 U.S.P.Q.2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar,* 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163. There is no *in haec verba* requirement, claim limitations can be supported in the specification through express, implicit, or inherent disclosure. M.P.E.P. § 2163 (I)(B).

With respect to claims 24-39, the Office has asserted that the claims read on preparing a "gutless" adenoviral vector. In the Office Action dated October 6, 2004, the Office alleged that "a vector with minimal adenoviral sequence is not supported by the specification." Essentially the same allegations were made concerning claim 40. The Office has acknowledged that the specification as a whole refers to deletions of all or part of E1, E2, E3 and/or E4 and provides examples of such. *See* Office Action dated July 5, 2005, at 5.

Applicants previously pointed to examples of the use of the presently claimed methods to prepare vectors having various configurations that are described in the Examples section of the Specification. Applicants also pointed out that the Specification teaches that "a method according to the invention can enable a recombinant adenoviral vector lacking all or part of the E1, E2, E3, and/or E4 regions to be prepared." The Office responded by alleging that this teaching is not commensurate with the claims as written. The Office has referred to Figure 1 of the specification, and asserts that "[w]hen even all of E1, E2, E3, and E4 are deleted, substantial virus genome remains." *See* Office Action dated July 5, 2005, at 3. However, a closer consideration of Figure 1 shows that the Office is in error on this point.

It appears that the Office has misapprehended the nature of the adenoviral genome and the description of the presently claimed vectors in the Specification. Considering Figure 1, it may be noted that an adenovirus genome can be divided into 100 map units as illustrated by the scale that appears below the r-strand and l-strand. The native genome is about 36 kb long. *See, e.g.*, Specification at 2, lines 5-6. Each unit on the scale represents about 360

bases of the genome. Also, using the convention in the field, on Figure 1 each gene region is indicated with various symbols. The promoter is indicated beginning with a square bracket at the promoter location. Exon locations are shown by bars. And the terminus of a gene is indicated with an arrow head in line with the promoter that also points in the direction of the coding sequence, thereby indicating which strand encodes the respective gene in the sense direction. Gene regions are also labeled according to the convention in the field as consisting of the segment of the genome containing sequences from the promoter(s) to the termini of the genes comprising each of the groupings.

From the vicinity of the promoter to the termination of the genes in each of the E1, E2, E3, and E4 gene regions, these regions together span essentially the entire adenoviral genome with the exception of the encapsidation region and the 5' and 3' ITR's recited in the claims. In particular, E1A spans from about unit 1 to about unit 5. E1B spans from about unit 5 to about unit 11. E2B, encoded on the opposite l-strand, spans from about unit 11 to about unit 76, with E2A contained within this region. E3 spans from about unit 77 to about unit 87. E4, encoded on the opposite l-strand, spans from about unit 91 to about 99. Nothing in the Specification suggests that these regions are defined as having boundaries other than the boundaries indicated on Figure 1. See, for example, the curly brackets that define E2, E3 and E4 and the bars denoting E1A and E1B in Figure 1.

Deleting all of the E1, E2, E3, and E4 early gene regions including all the sequence from the promoters to the gene termini would leave only the approximately map 4 unit (that is about 4% of the genome) segment between E3 and E4 as the only internal segment of notable length together with various small segments between genes. The segments between the four early gene regions by themselves encode no whole functional genes.

Thus, contrary to the apparent misapprehension by the Office, the Specification in teaching that "a method according to the invention can enable a recombinant adenoviral vector lacking all or part of the E1, E2, E3, and/or E4 regions to be prepared" describes preparation of vectors wherein one or more regions are wholly or partly deleted including some in which substantially all of the genome is lacking, in each case with the preferable exception of the encapsidation region and the 5' and 3' ITR's as recited in the claims.

The Office is partially correct when it asserts that there are other regions besides E1, E2, E3, and/or E4. Predominantly these include the various genes driven by the major late promoter. However, Figure 1 illustrates that these other regions are all overlapping one or more of the E1, E2, E3, and E4 regions. A person of ordinary skill would appreciate that the overlapping genes would be deleted in any complete deletion of E1, E2, E3, and E4. The person of ordinary skill would have no compelling reason to retain any of the small interstitial segments between regions when deleting all of E1, E2, E3, and E4.

This is further supported in the Specification where it clearly describes that the deletions are not limited to only all or part of E1, E2, E3, and/or E4. For example, the Specification broadly states that "In accordance with the objectives pursued by the present invention, a method according to the invention is carried out for the preparation of a recombinant viral vector which is defective for replication." Specification at page 10, line 38 to page 11, line 2. A viral vector which is defective for replication is defined in the Specification, without limitation, as follows: "Generally, the genome of these defective vectors lacks one or more genes essential for replication, early genes and/or late genes. They may be wholly or partly deleted or rendered non-functional by mutation . . ." *Id.* at page 11, lines 4-9 (emphasis added).

Thus, the deletion of all or part of E1, E2, E3, and E4 as discussed above is clearly not intended to be limiting. The adenoviral genome can lack all or part of any early or late gene region. The only preferred restriction on deletion is described in the Specification as follows: "Although the insertion region of the exogenous sequence may be located in any position of the viral genome, it is preferable to avoid the regions acting in *cis* necessary for replication. These regions comprise, in particular, . . . the 5' and 3' ITRs and the encapsidation region as regards adenoviruses." Specification at page 9, lines 22-29. This preference is reflected in the recitation of the present claims, which state that the adenoviral vector comprises the encapsidation region and the 3' and 5'ITRs.

For at least the foregoing reasons, the description of the Specification with respect to the types of adenovirus that may be prepared by the claimed methods is entirely commensurate with the claims as previously presented.

The foregoing notwithstanding, without acceding to the alleged basis of the rejection, but simply in order to expedite issuance of a patent using claim language that the Office has acknowledged is described in the Specification, claims 24 and 40 have been amended to recite that the recombinant adenoviral vector comprises the adenoviral genome lacking all or part of the E1, E2, E3 and/or E4 regions. The Office has acknowledged that the Specification "refers to deletions of all or part of E1, E2, E3 and E4 and provides examples of such."

Thus, the claims as currently presented are clearly described by the Specification and withdrawal of the rejections is respectfully requested.

Interview Summary

Applicants' representative thanks the Examiner for the courtesy of interviews conducted on October 4 and 5, 2005. The claims and the issues underlying the current

rejection were discussed in order that the position of the Office might be better understood. Agreement as to the rejection was not reached.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL PC

Date: October 6, 2005

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